AF 1617

Docket No.: H1890.0201
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:

Gary D. Hodgen et al.

Application No.: 09/313,628

Filed: May 18, 1999

Art Unit: 1617

For: CONTROL OF SELECTIVE ESTROGEN RECEPTOR MODULATORS

Examiner: Gregory W. Mitchell

REPLY BRIEF

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This short brief is submitted to reply to various arguments made in the Examiner's Answer.

The essence of the Examiner's rejection, as characterized in the Examiner's Answer, is that since both SERMs and progestins are known as contraceptive agents and since oral contraceptives are known to cause bleeding, it would be obvious to combine them and optimize the dosages of the SERM and progestin to effectuate the minimal amount of bleeding possible. There are several problems with this position.

It will be appreciated that the rejection is predicated on SERMs being known as contraceptive agents for human beings. There is no factual basis for this assertion.

There is nothing in the record which shows that a SERM was known to be an effective contraceptive agent in the pre-menopausal human female on the effective date of this application. Jones and Basu[1], do not deal with human beings. On the other hand, there is considerable evidence of record that indicates that it is not possible to extend results achieved with lower animals to human beings. The Greenblatt reference, albeit predating Jones and Basu, indicates one cannot analogize between rats and women. There is nothing in either Jones or Basu which suggest their teachings can be extended to human beings and therefore the attempt to dismiss Greenblatt based on date is off the point - Jones and Basu do not have a different teaching than Greenblatt. The Clark reference likewise points out that it is not appropriate to apply teachings cross-species. While it is true that Clark does also say that the differences are "more likely to be due to differences in treatment protocols", the very next paragraph explains further that the protocol with rats involved high doses over long periods of time relative to the short cycle length of the rat. Also, that paragraph also refers to an article by Docke as pointing out "the cycling rat is not comparable to an ovulatory woman". It cannot be gainsaid that Clark states "these drugs have been used extensively in woman for the induction of ovulation (clomiphene)" (page 1039) and that "in humans, clomiphene induces ovulation in an ovulatory woman" (page 1041). Indeed, the SERM clomiphene is well known under the trademark Clomid, a potent fertility preparation.

A copy of the Shane article is attached to the Examiner's Answer whereas only an abstract was previously of record. The full article makes reference to reports in 1974 about the use of danazol as a contraceptive. Applicants will waive their right to insist on reopening of prosecution to properly make the full article of record if the attached article by Webb (1992) and Woman's Health (1999), both of which show that

[1] A copies of Basu is attached to the Examiner's Answer while previously only an abstract was of record. Since the full article does not have teachings beyond the abstract, any objection to the late citation is waived.

danazol is currently recognized not to have contraceptive properties, are considered as being of record.

Applicants have stated that the early belief was that SERMs had contraceptive effect in humans, but contrary to that early belief, the art learned that SERMs were actually fertility agents in humans, giving rise to "runaway" endogenous estrogen production and thereby inducing ovulation, and the over production of the endogenous estrogen exaggerated the estrogen bleeding side effect. The art of record supports that statement.

The claimed invention is based on the discovery that there is an amount of a progestogenic agent which permits the SERM to be used for contraceptive purposes rather than fertility inducing purposes and that this amount modulates the bleeding side effect of the SERM.

The Examiner's position that it would be obvious to combine compounds each of which are taught by the prior art to be useful for the same purpose to form a composition to be used for the same purpose thus lacks a factual basis. While the art teaches that SERMs can be used as a contraceptive for lower animals, there is nothing in the record which shows that the SERMs were recognized to be useful as a contraceptive for the pre-menopausal human female, the subject of the claims on appeal, as of the effective date of this application, and quiet to the contrary, the record indicates that the SERMs are fertility agents in the pre-menopausal human female.

Even if there was a teaching that both the SERM and progestogenic agent were useful for the same purpose, and there is not, there is nothing in the art which teaches or suggest that the amount of progestogenic agent will have any effect whatsoever on the amount of bleeding of the SERM. The Examiner suggests that while

the skilled person would seek to minimize the bleeding side effect by optimizing the dosages of the SERM and progestogenic agent. That, however, is simply an invitation to experiment using hindsight because nothing teaches those skilled in the art that the relative amounts of anything effects bleeding. It is well established that it is unobvious to optimize a parameter which has not previously been recognized as result effecting. Further, combining two entities each of which is characterized by a bleeding side effect in such a way as to reduce bleeding is counterintuitive and unobvious. The claims on appeal call for a contraceptive amount of a SERM and the use of an amount of progestogenic agent effective to ameliorate or eliminate the bleeding side effect of the contraceptive effective amount of the SERM. There is nothing which teaches or suggest that any amount of the progestogenic agent which will ameliorate or eliminate the bleeding side effect of the amount of the SERM being employed. Quite to the contrary, the expectation is that bleeding will be exaggerated because the added agent induces bleeding and superposing it on something (the SERM) which already causes bleeding would never be expected to reduce the overall bleeding rate.

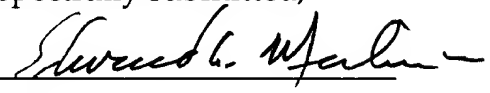
The Examiner's assertion that Applicant is not claiming a method of ameliorating or eliminating bleeding side effects is clearly wrong because the claims specifically call for the use of a progestogenic agent in an amount effective to ameliorate or eliminate the bleeding side effects of the SERM being employed.

In summary, the art of record teaches the use of SERMs as fertility (anti-contraceptive) agents in the human female and fails to teach or suggest that the SERMs can be used as a contraceptive agent in the human female if there is additional use of a progestogenic agent in an amount to ameliorate or eliminate the bleeding side effect, such as uterine bleeding, that otherwise accompany human use of SERMs. None of the references, whether considered alone or in combination, would motivate one skilled in the art to combine them to realize the invention recited in the claims on appeal.

The Examiner's rejection should be reversed.

Dated: August 12, 2005

Respectfully submitted,

By 

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